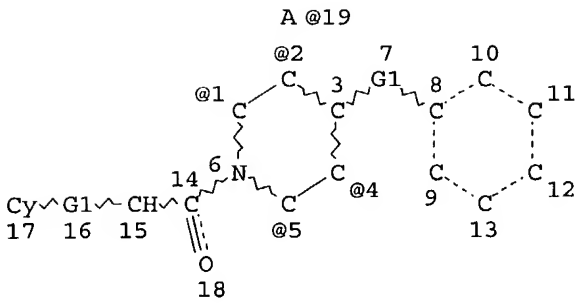


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SEARCH TIME: 00.00.01

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FULL SCREEN SEARCH COMPLETED -   2049 TO ITERATE

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SEARCH TIME: 00.00.01

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 26 Jul 2004 VOL 141 ISS 5

FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d bib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80652 CAPLUS
DN 140:146007
TI Preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors.
IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009550	A1	20040129	WO 2003-IB2876	20030707
US 2004063759	A1	20040401	US 2003-616844	20030708

PI WO 2004009550 A1 20040129 WO 2003-IB2876 20030707
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US 2004063759 A1 20040401 US 2003-616844 20030708
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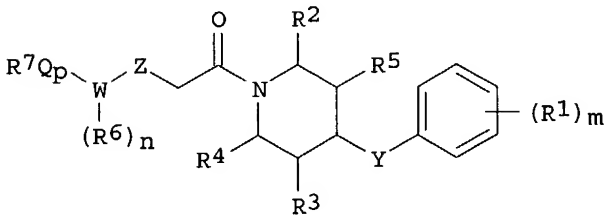

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AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR8; R8 = H, alkyl; Z = O, NR9; R9 = H, alkyl, Ac; R1 = H, halo, cyano, NO2, CF3, OCF3, alkyl, OH, alkylcarbonyloxy, alkoxy; R2-R5 = H, (halo)alkyl; R6 = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R7 = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥1 of R2-R5 =

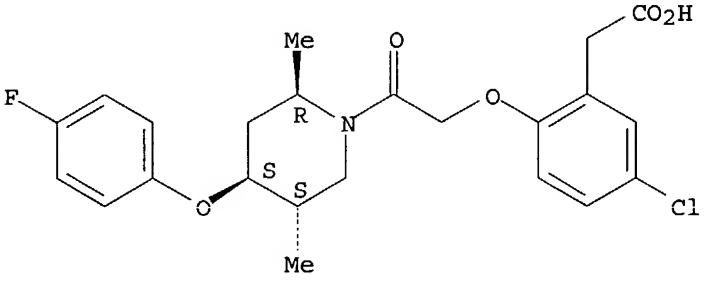
alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH2Cl2 was treated with Et3N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give [5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC50 <10 μM.

IT **651301-01-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651301-01-8 CAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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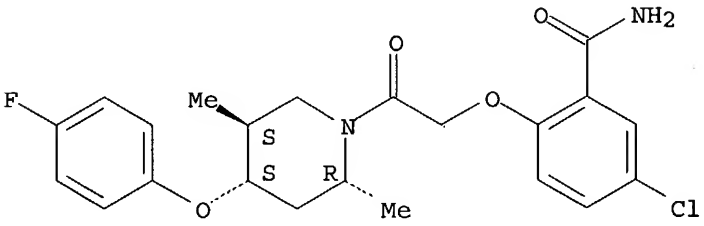
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651300-98-0 CAPLUS

CN Benzamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

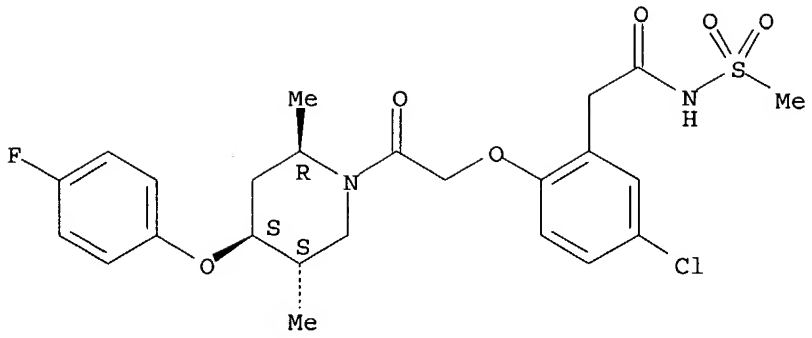
Relative stereochemistry.



RN 651301-03-0 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 651301-04-1 CAPLUS
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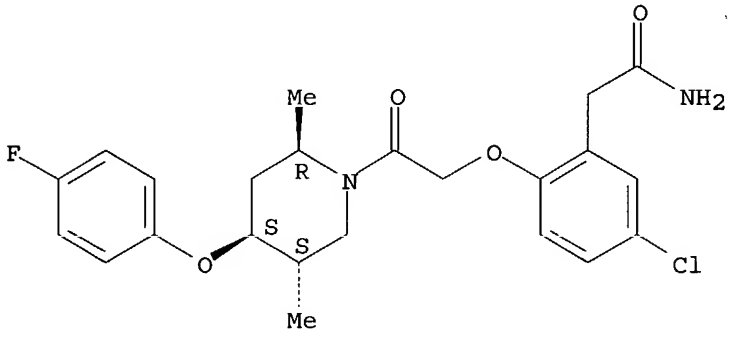
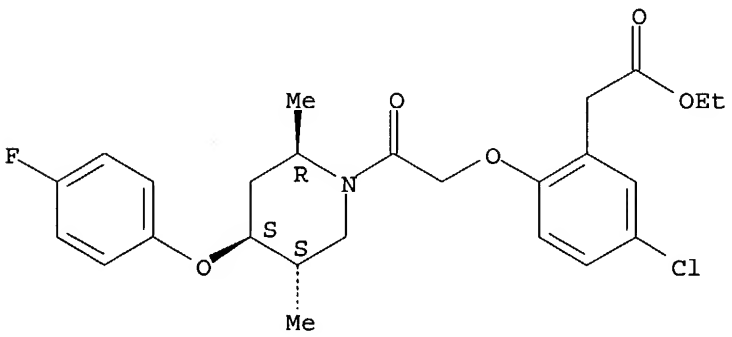
Relative stereochemistry.

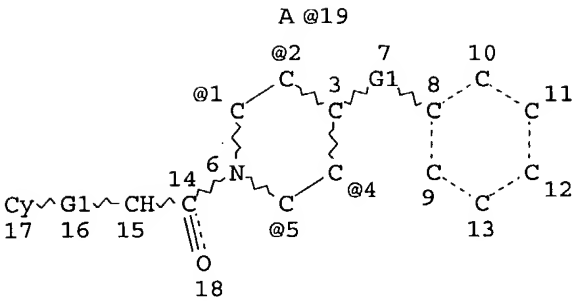


IT **651301-33-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)
RN 651301-33-6 CAPLUS
CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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VPA 19-2/1/5/4 U
ENTER (DIS), GRA, NOD, BON OR ?:end
L1   STRUCTURE CREATED

=> s l1
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SAMPLE SCREEN SEARCH COMPLETED -    101 TO ITERATE

100.0% PROCESSED     101 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          1418 TO     2622
PROJECTED ANSWERS:                0 TO        0

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FULL SCREEN SEARCH COMPLETED -   2049 TO ITERATE

100.0% PROCESSED    2049 ITERATIONS                              5 ANSWERS
SEARCH TIME: 00.00.01

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=> fil caplus
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   156.68     156.89

FILE 'CAPLUS' ENTERED AT 09:48:46 ON 26 JUL 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 26 Jul 2004  VOL 141 ISS 5
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FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 1 L3

=> d bib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80652 CAPLUS
DN 140:146007
TI Preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors.
IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009550	A1	20040129	WO 2003-IB2876	20030707
US 2004063759	A1	20040401	US 2003-616844	20030708

PI WO 2004009550 A1 20040129 WO 2003-IB2876 20030707
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US 2004063759 A1 20040401 US 2003-616844 20030708
PRAI US 2002-397108P P 20020718
OS MARPAT 140:146007
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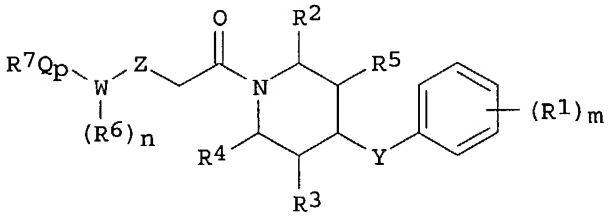

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AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR8; R8 = H, alkyl; Z = O, NR9; R9 = H, alkyl, Ac; R1 = H, halo, cyano, NO2, CF3, OCF3, alkyl, OH, alkylcarbonyloxy, alkoxy; R2-R5 = H, (halo)alkyl; R6 = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R7 = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥1 of R2-R5 =

alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH2Cl2 was treated with Et3N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give [5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC50 <10 μM.

IT **651301-01-8P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
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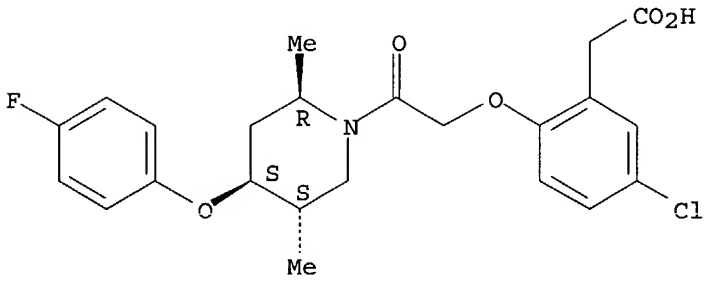
RN 651301-01-8 CAPLUS

CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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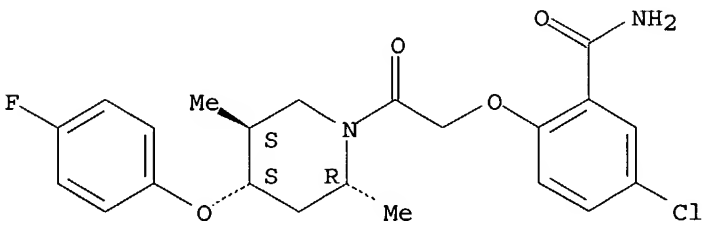
RN 651300-98-0 CAPLUS

CN Benzamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, rel- (9CI) (CA INDEX NAME)

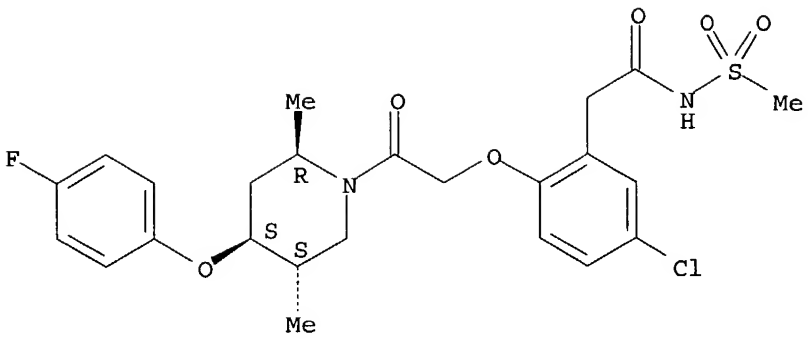
Relative stereochemistry.



RN 651301-03-0 CAPLUS

CN Benzeneacetamide, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 651301-04-1 CAPLUS
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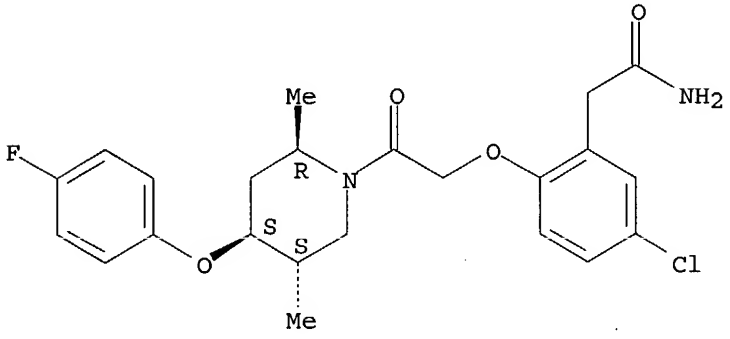
Relative stereochemistry.



IT **651301-33-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
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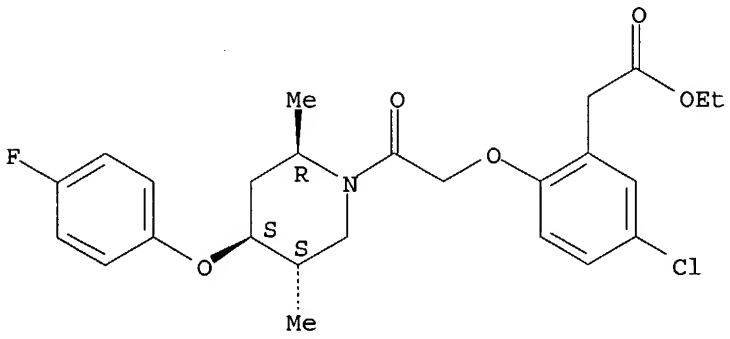
CN Benzeneacetic acid, 5-chloro-2-[2-[(2R,4S,5S)-4-(4-fluorophenoxy)-2,5-dimethyl-1-piperidinyl]-2-oxoethoxy]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L5 HAS NO ANSWERS
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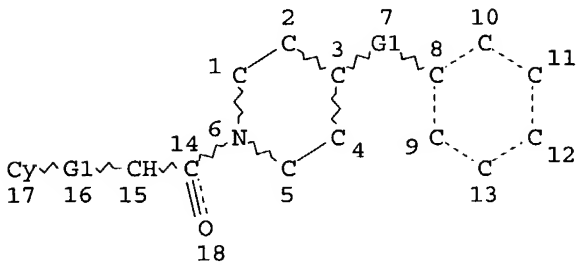

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RSPEC 2 8
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.02

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L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80652 CAPLUS
DN 140:146007
TI Preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors.
IN Blumberg, Laura Cook; Brown, Matthew Frank; Hayward, Matthew Merrill; Poss, Christopher Stanley
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004009550	A1	20040129	WO 2003-IB2876	20030707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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PRAI US 2002-397108P P 20020718
OS MARPAT 140:146007
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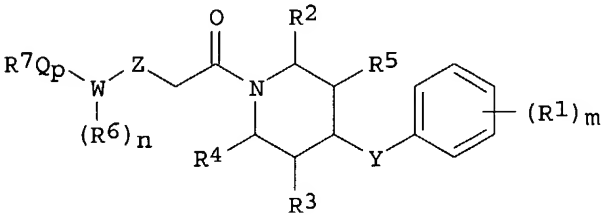


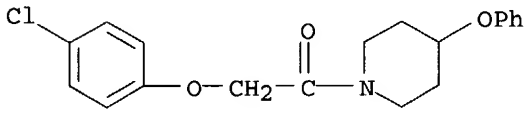
I

AB Title compds. [I; m = 1-5; n = 0-4; p = 0-1; Q = alkyl; W = aryl, heteroaryl; Y = O, NR8; R8 = H, alkyl; Z = O, NR9; R9 = H, alkyl, Ac; R1 = H, halo, cyano, NO2, CF3, OCF3, alkyl, OH, alkylcarbonyloxy, alkoxy; R2-R5 = H, (halo)alkyl; R6 = H, halo, (halo)alkyl, cyano, alkoxy, aminocarbonyl, carboxy, alkylcarbonyl, (halo)alkoxy; R7 = H, halo, (halo)alkyl, dialkylaminoalkylaminocarbonyl, alkoxy, aminocarbonyl, ureido, aminosulfonyl, alkylsulfonylaminoalkylamino, aminosulfonylamino, heteroaryloxy, ureidoalkylaminocarbonyl, etc.; ≥1 of R2-R5 = alkyl], were prepared Thus, 2-(2-amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone (preparation given) in CH2Cl2 was treated with Et3N and Ph chloroformate, The reaction was stirred at ambient temperature for 4 h, concentrated in vacuo, and the resulting residue dissolved in methanol followed by bubbling in ammonia gas for 10 min and stirred overnight at ambient temperature to give [5-chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea. I inhibited chemotaxis with IC50 <10 μM.

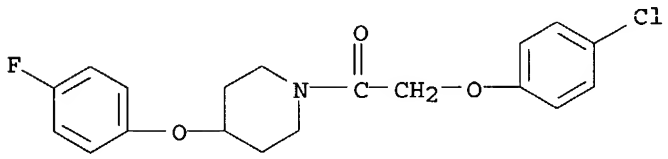
IT **651300-89-9P**, 2-(4-Chlorophenoxy)-1-(4-phenoxypiperidin-1-yl)ethanone **651300-90-2P**, 2-(4-Chlorophenoxy)-1-[4-(4-

fluorophenoxy)piperidin-1-yl]ethanone **651300-92-4P**, 5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]benzamide **651300-93-5P**, [5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]urea **651301-05-2P**, [5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]acetic acid **651301-07-4P**, N-[[5-Chloro-2-[2-[4-(4-fluorophenoxy)piperidin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

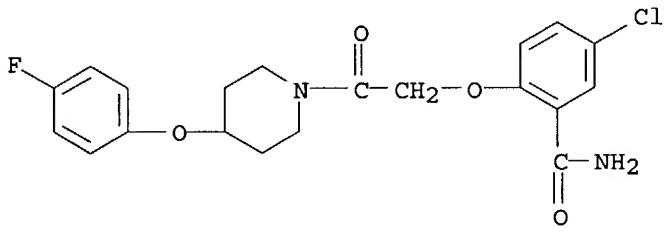
RN 651300-89-9 CAPLUS
CN Piperidine, 1-[(4-chlorophenoxy)acetyl]-4-phenoxy- (9CI) (CA INDEX NAME)



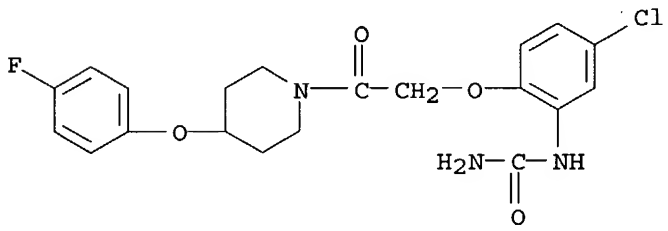
RN 651300-90-2 CAPLUS
CN Piperidine, 1-[(4-chlorophenoxy)acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



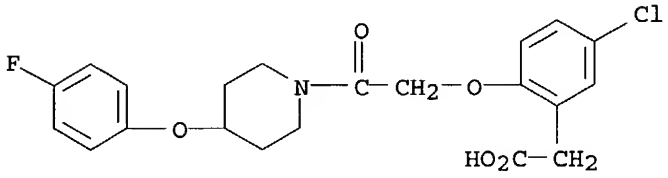
RN 651300-92-4 CAPLUS
CN Benzamide, 5-chloro-2-[2-[4-(4-fluorophenoxy)-1-piperidinyl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



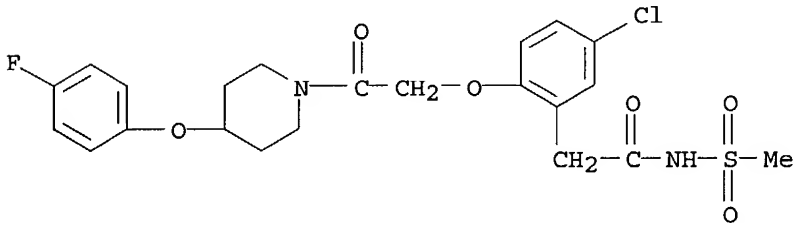
RN 651300-93-5 CAPLUS
CN Piperidine, 1-[[2-[(aminocarbonyl)amino]-4-chlorophenoxy]acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



RN 651301-05-2 CAPLUS
CN Benzeneacetic acid, 5-chloro-2-[2-[4-(4-fluorophenoxy)-1-piperidinyl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

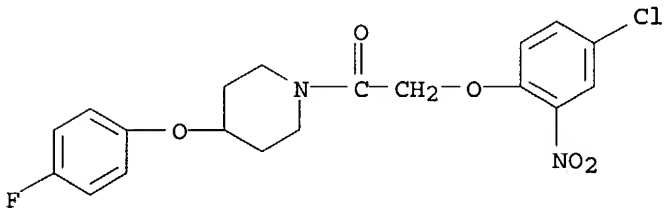


RN 651301-07-4 CAPLUS
CN Benzeneacetamide, 5-chloro-2-[2-[4-(4-fluorophenoxy)-1-piperidinyl]-2-oxoethoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

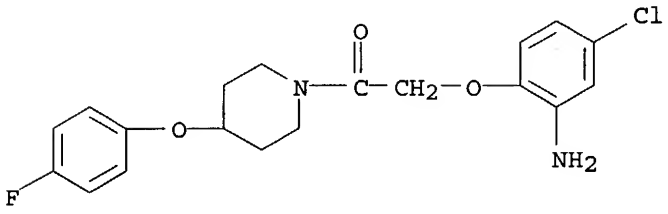


IT **651301-45-0P**, 2-(4-Chloro-2-nitrophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone **651301-48-3P**, 2-(2-Amino-4-chlorophenoxy)-1-[4-(4-fluorophenoxy)piperidin-1-yl]ethanone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylketones as as selective inhibitors of macrophage inflammatory protein 1α (MIP-1α) binding to CCR1 chemokine receptors)

RN 651301-45-0 CAPLUS
CN Piperidine, 1-[(4-chloro-2-nitrophenoxy)acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



RN 651301-48-3 CAPLUS
CN Piperidine, 1-[(2-amino-4-chlorophenoxy)acetyl]-4-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:97412 CAPLUS
DN 138:153539
TI Preparation of 2-(piperidin-1-yl)acetamides as NMDA receptor antagonists
IN Domany, Gyoergy; Horvath, Csilla; Farkas, Sandor; Barta Szalai, Gisella; Nagy, Jozsef; Kolok, Sandor; Kovacs Bozo, Eva; Borza, Istvan; Vago, Istvan; Bielik, Attila; Szendrei, Mrs. Gyorgyi Ignaczne; Keseru, Gyorgy
PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003010159	A1	20030206	WO 2002-HU71	20020723
WO 2003010159	C1	20040212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

761940

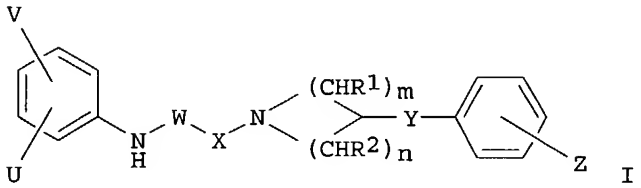
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EE 200400058	A	20040415	EE 2004-58	20020723
EP 1409477	A1	20040421	EP 2002-753161	20020723

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI HU 2001-3055	A	20010724	
HU 2002-2213	A	20020710	
WO 2002-HU71	W	20020723	

OS MARPAT 138:153539
GI



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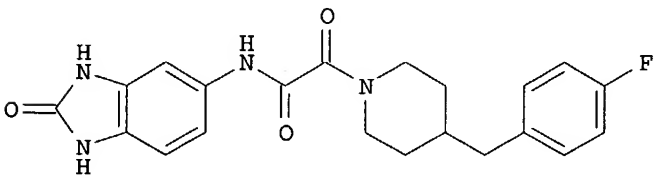


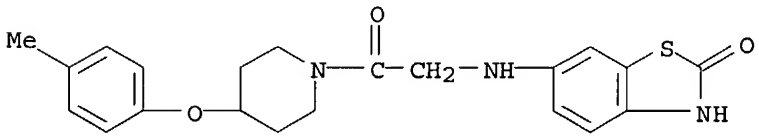
II

AB The title compds. I [wherein V and U = independently H, halo, OH, CN, NO2, NH2, alkylsulfonyloxy, carboxyl, CF3, CF3O, alkyl-SO2-NHCH2, NH2-(CH2)1-4-SO2NH, NH2-(CH2)1-4-CONH, sulfamoyl, CHO, aminomethyl, HOCH2, alkyl, alkoxymethyl, halo-CH2, tetrazolyl, alkoxy(carbonyl), alkanoyloxy,

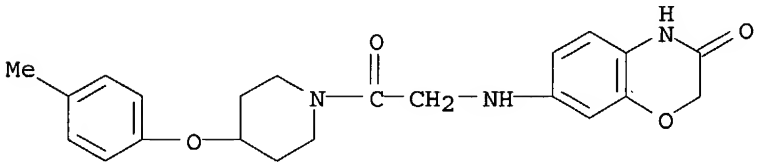
Ph, (un)substituted alkylamino, arylamino, aralkylamino, alkylsulfonamido, alkanoylamido, arylsulfonamido, or alkoxy groups; or the neighboring V and U together form (un)substituted 4-7 membered ring with the atoms attached; W and X = independently CO, CH2, or CH-alkyl; Y = O, (cyclo)alkylene, alkynylene, aminocarbonyl, NH, N-alkyl, CH2O, CH(OH), or OCH2; Z = H, halo, NO2, NH2, alkyl, alkoxy, CN, CF3, OH, or CO2H; R1 and R2 = independently H or alkyl; or R1 and R2 together form (un)substituted C1-C3 bridge; n and m = independently 0-3 with restriction that n and m ≠ 0 at the same time; with provisos] and optical antipodes, racemates, or pharmaceutically acceptable salts thereof are prepared as NMDA receptor antagonists, and moreover most of the compds. are selective antagonist of NR2B subtype of NMDA receptor. For example, 2-[4-(4-fluorobenzyl)piperidin-1-yl]-2-oxoacetic acid (prepn given) was treated with 5-amino-1,3-dihydroindol-2-one in DMF in the presence of Et3N and HBTU to afford the acetamide II (48%). II showed IC50 of 0.0007 μM against NMDA in rat. Formulations containing I as an active ingredient were also described.

IT **496057-62-6P 496057-66-0P 496058-00-5P**
496058-03-8P 496058-04-9P 496058-06-1P
496058-14-1P 496058-15-2P 496058-17-4P
496058-18-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NMDA receptor antagonist; preparation of piperidinylacetamides by coupling reactions as NMDA receptor antagonists)

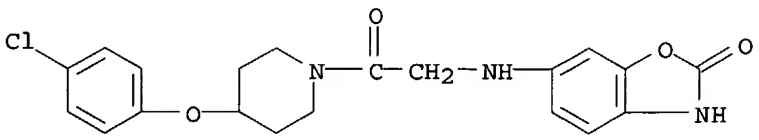
RN 496057-62-6 CAPLUS
CN Piperidine, 1-[[(2,3-dihydro-2-oxo-6-benzothiazolyl)amino]acetyl]-4-(4-methylphenoxy)- (9CI) (CA INDEX NAME)



RN 496057-66-0 CAPLUS
CN Piperidine, 1-[[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-7-yl)amino]acetyl]-4-(4-methylphenoxy)- (9CI) (CA INDEX NAME)

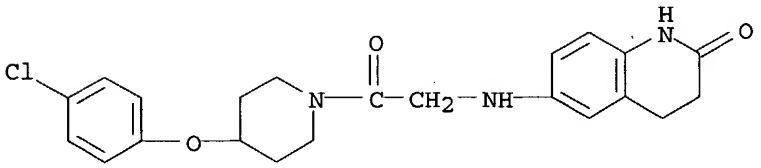


RN 496058-00-5 CAPLUS
CN Piperidine, 4-(4-chlorophenoxy)-1-[[(2,3-dihydro-2-oxo-6-benzoxazolyl)amino]acetyl]- (9CI) (CA INDEX NAME)

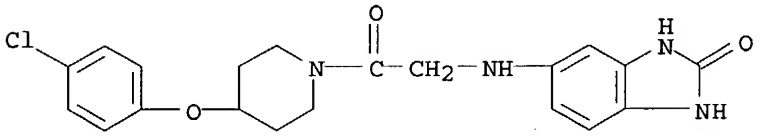


RN 496058-03-8 CAPLUS

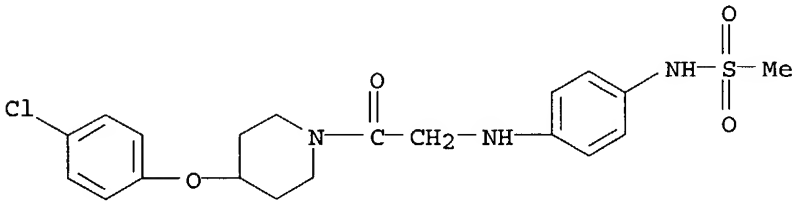
CN Piperidine, 4-(4-chlorophenoxy)-1-[[(1,2,3,4-tetrahydro-2-oxo-6-quinolinyl)amino]acetyl]- (9CI) (CA INDEX NAME)



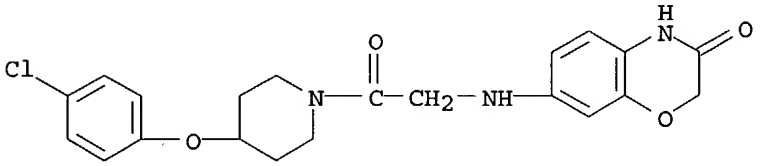
RN 496058-04-9 CAPLUS
CN Piperidine, 4-(4-chlorophenoxy)-1-[[(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)amino]acetyl]- (9CI) (CA INDEX NAME)



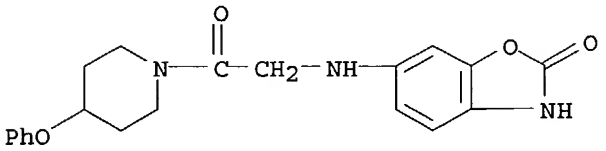
RN 496058-06-1 CAPLUS
CN Piperidine, 4-(4-chlorophenoxy)-1-[[[4-[(methylsulfonyl)amino]phenyl]amino]acetyl]- (9CI) (CA INDEX NAME)



RN 496058-14-1 CAPLUS
CN Piperidine, 4-(4-chlorophenoxy)-1-[[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-7-yl)amino]acetyl]- (9CI) (CA INDEX NAME)

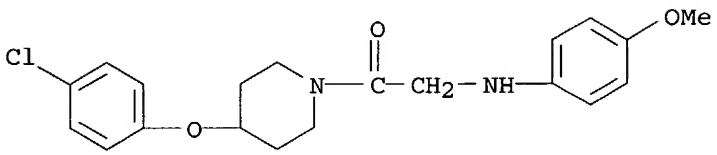


RN 496058-15-2 CAPLUS
CN Piperidine, 1-[[(2,3-dihydro-2-oxo-6-benzoxazolyl)amino]acetyl]-4-phenoxy- (9CI) (CA INDEX NAME)

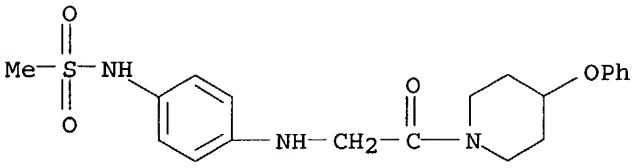


RN 496058-17-4 CAPLUS

CN Piperidine, 4-(4-chlorophenoxy)-1-[[(4-methoxyphenyl)amino]acetyl]- (9CI) (CA INDEX NAME)



RN 496058-18-5 CAPLUS
CN Piperidine, 1-[[[4-[(methylsulfonyl)amino]phenyl]amino]acetyl]-4-phenoxy- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

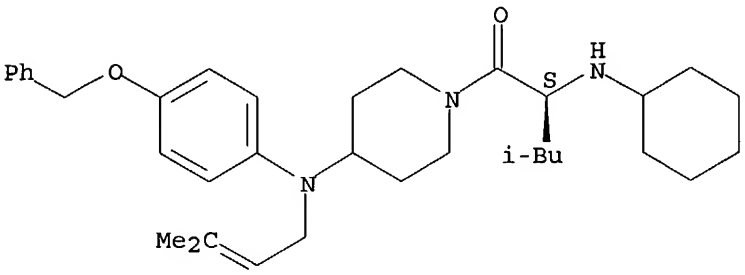
L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:589098 CAPLUS
DN 131:331730
TI Synthesis of a Series of 4-Benzyloxyaniline Analogs as Neuronal N-Type Calcium Channel Blockers with Improved Anticonvulsant and Analgesic Properties
AU Hu, Lain-Yen; Ryder, Todd R.; Rafferty, Michael F.; Feng, M. Rose; Lotarski, Susan M.; Rock, David M.; Sinz, Michael; Stoehr, Sally J.; Taylor, Charles P.; Weber, Mark L.; Bowersox, S. Scott; Miljanich, George P.; Millerman, Elizabeth; Wang, Yong-Xiang; Szoke, Balazs G.
CS Departments of Chemistry Neuroscience Therapeutics and Pharmacokinetics Dynamics and Metabolism, Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SO Journal of Medicinal Chemistry (1999), 42(20), 4239-4249
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB In this article, the rationale for the design, synthesis, and biol. evaluation of a series of N-type voltage-sensitive calcium channel (VSCC) blockers is described. N-Type VSCC blockers, such as ziconotide, have shown utility in several models of stroke and pain. Modification of the previously reported lead led to several 4-(4-benzyloxylphenyl)piperidine structures with potent in vitro and in vivo activities. In this series, the most interesting compound, (S)-2-amino-1-{4-[(4-benzyloxy-phenyl)-(3-methyl-but-2-enyl)-amino]-piperidin-1-yl}-4-methyl-pentan-1-one (I), blocked N-type calcium channels (IC50 = 0.67 μM in the IMR32 assay) and was efficacious in the audiogenic DBA/2 seizure mouse model (ED50 = 6 mg/kg, i.v.) as well as the antiwrithing model (ED50 = 6 mg/kg, i.v.). Whole-cell voltage-clamp electrophysiol. expts. demonstrated that compound I blocked N-type Ca2+ channels and Na+ channels in superior cervical ganglion neurons at similar concns. Compound I, which showed superior in vivo efficacy, stands out as an interesting lead for further development of neurotherapeutic agents in this series.
IT **250237-03-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
(synthesis of 4-benzyloxyaniline analogs as neuronal N-type calcium channel blockers with improved anticonvulsant and analgesic properties)

RN 250237-03-7 CAPLUS

CN 4-Piperidinamine, 1-[(2S)-2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methyl-2-butenyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

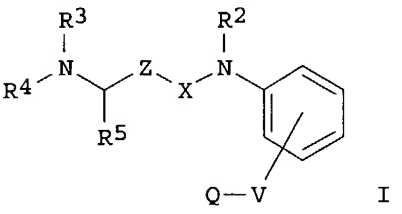


RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:126886 CAPLUS
DN 130:196584
TI Preparation of aniline derivatives as calcium channel blockers
IN Hu, Lain-Yen; Rafferty, Michael Francis; Ryder, Todd Robert
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9907689	A1	19990218	WO 1998-US15907	19980729
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9887627	A1	19990301	AU 1998-87627	19980729
	ZA 9807144	A	19990510	ZA 1998-7144	19980807
	US 6251918	B1	20010626	US 1999-402196	19990929
	US 2001023249	A1	20010920	US 2001-769798	20010125
	US 6495715	B2	20021217		
	US 2003060632	A1	20030327	US 2002-252854	20020923
PRAI	US 1997-55251P	P	19970811		
	US 1998-82358P	P	19980420		
	WO 1998-US15907	W	19980729		
	US 1999-402196	A3	19990929		
	US 2001-769798	A3	20010125		

OS MARPAT 130:196584
GI



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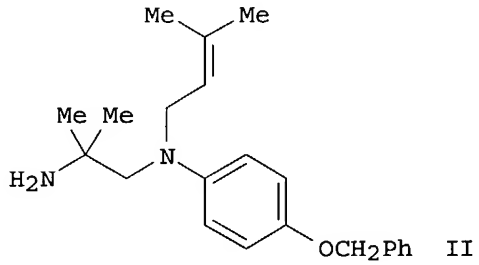
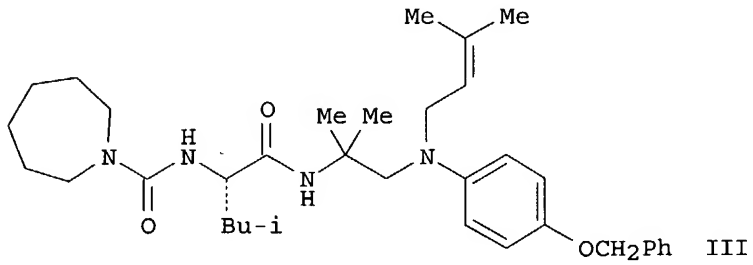


II



III

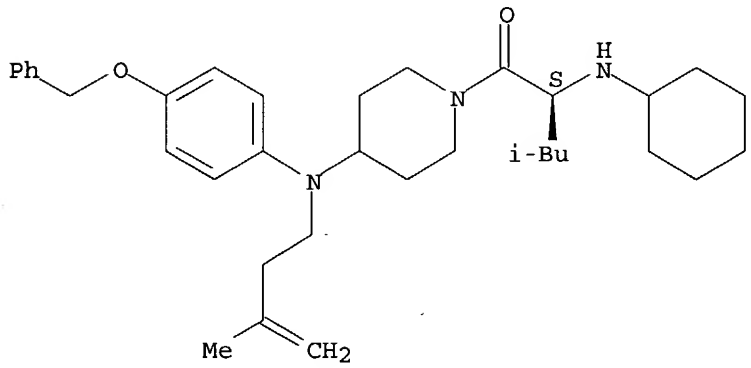
AB The invention provides compds. that block calcium channels. In

particular, the invention claims compds. I [Z = CH2 or CO; X = cycloalkylene, (un)substituted heterocycloalkylene, imino or iminoalkylene, certain piperidinediyl or pyrrolidinediyl radicals or their alkylene derivs.; Q = H, (un)substituted aryl, heteroaryl, cycloalkyl, alkyl, heterocycloalkyl; V = O(CH2)n or (CH2)nO, O, (CH2)n, CH:CH, NH(CH2)n or (CH2)nNH or derivs.; R2 = H, alkenyl, cycloalkenyl, (un)substituted Ph, alkyl, cycloalkyl, or Ph; R3 = H, alkyl, alkenyl; R4 = H, cyclo-(CH2)mNCO, alkyl, alkenyl, (un)substituted Ph, heteroaryl, or cycloalkyl; or NR3R4 = 5- to 7-membered ring with an optional addnl. heteroatom; R5 = alkyl, (un)substituted Ph or heteroaryl; m = 1-3; n = 0-3] and their pharmaceutically acceptable salts, esters, amides, and prodrugs. The invention also provides methods of using the compds. to treat stroke, cerebral ischemia, head trauma, or epilepsy, and to pharmaceutical compns. that contain the compds. Over 50 synthetic examples are given, and these plus a large number of addnl. invention compds. are specifically claimed. For instance, N-BOC-α-aminoisobutyric acid underwent amidation with 4-benzyloxyaniline, followed by reduction of the amide with diborane, N-alkenylation with 4-bromo-2-methyl-2-butene, and acidic deprotection to remove BOC, to give intermediate II. In a sep. preparation, H-Leu-OCH2Ph was treated with triphosgene and hexamethylenamine, then deprotected, to give Hac-Leu-OH (III; Hac = hexamethylenaminocarbonyl). Coupling of II with III using HBTU and DIPEA in DMF gave title compound IV. The latter blocked calcium flux through N-type Ca2+ channels in IMR-32 neuronal tumor cells in vitro, with IC50 of 0.26 μM. Selected compds. gave 20-100% protection of mice from tonic seizures in a sound chamber, at doses of 10-30 mg/kg i.v.

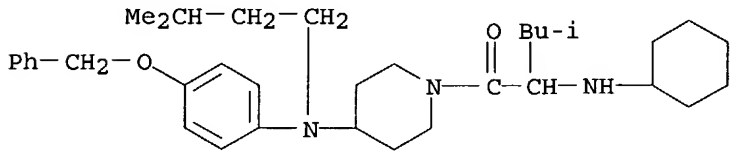
IT **220737-62-2P 220738-14-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aniline derivs. as calcium channel blockers)

RN 220737-62-2 CAPLUS
CN 4-Piperidinamine, 1-[(2S)-2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methyl-3-butenyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220738-14-7 CAPLUS
CN 4-Piperidinamine, 1-[2-(cyclohexylamino)-4-methyl-1-oxopentyl]-N-(3-methylbutyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT